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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,229	04/06/2001	Zvia Agur	Q63893	7712

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	11

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,229	AGUR ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-167 and 332-349* is/are pending in the application.

4a) Of the above claim(s) *118-167* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-117 and 332-349* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/6/01* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *07 July 2003* is: a)☐ approved b)☒ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Election/Restrictions

Claims 118-167 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

This application contains claims 118-167, drawn to a nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

An action on the merits of elected claims 66-117 and 332-349 follows.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All objections and rejections not reiterated below are hereby withdrawn.

Information Disclosure Statement

Applicant is again reminded of the duty to disclose to the Office all information known to that individual to be material to patentability, as set forth under 37 CFR 1.56. It is noted that numerous references are cited throughout the specification; however, no IDS has been received by the examiner as of the date of this office action.

Applicant is again advised that listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP

§ 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Drawings

Proposed corrected drawings were received on 7/7/03. These drawings are not approved by the examiner for the following reasons:

The proposed changes to the Figure legends of Figures 8 and 9 would render the Figures incomprehensible. Removing the reference to color would result in Figures wherein the data is not identified at all. Applicant has not proposed replacing the color references with any other identification of data which would render the Figures comprehensible.

The proposed changes to Figure 2 are acceptable. It is noted that Figure 2 still shows compartments labeled "P", but that there is no description of a compartment "P" is the specification.

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: compartments labeled "P" are not described. A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

There is no proposed change to Figure 7, therefore the objection to Figure 7 is maintained. As previously set forth, Figure 7 has no Figure legends, and is therefore

incomprehensible. Proposed drawing corrections or corrected drawings are required in reply to this Office action to avoid abandonment of the application. The objections to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: in the "Brief Description" of Figure 2b, as added by amendment to page 71, the term "methodology" should be --methodology--. Appropriate correction is required.

The abstract of the disclosure is again objected to because it does not specifically describe the subject matter of the elected claims. Applicant has not filed a new or amended abstract, therefore the objection is maintained. Correction is required. See MPEP § 608.01(b).

Claim Objections

Amended claims 81 and 107 are objected to because of the following informalities: the term --the-- should be inserted between "is" and "same" in line 1 of each claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 92-117 and 341-349 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A system or model for modeling thrombopoietic lineage in a general human patient is new matter, as recited in claims 92 and 341. Original claims 92 and 341 recited modeling thrombopoietic lineage in a general patient, but did not recite a *human* patient. None of the original claims recited modeling anything in a human patient. Page 1 discloses a system for modeling progression of cells in patients, page 2 discloses doing so for "general patients". Pages 9 and 45 disclose modeling in an individual. Pages 73 and 75 disclose modeling for a general patient versus an individual patient. Nowhere does the originally field specification actually disclose modeling for a general *human* patient. As made clear by the prior art, modeling of thrombopoietic lineage may be performed for animals; in a veterinary setting, an animal is a "patients". Therefore a disclosure for modeling of thrombopoietic lineage in a patient or in a general patient is not necessarily a disclosure for modeling in a *human* patient. As neither the originally filed specification or claims taught or recited a general human patient, the claims recite new matter and are rejected.

Claim Rejections - 35 USC § 112

Examiner's note: The terms "contains", "containing", "include", "including", and any other bridging term which is not specifically defined in the specification recited in the claims is interpreted by the examiner to be open claim language, equivalent to "comprises" or "comprising".

Claims 66-117 and 332-349 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 7/7/03 have been fully considered but they are not persuasive. Arguments with regard to individual rejections are addressed below.

Claim 66 recites the phrase "realistic process progression model". Claims 67, 69, 93, 95, 333, 335, 342, and 344 recite the phrase "realistic progression of cells". Claim 92 recites the phrase "realistic process model". Claims 332 and 341 recite a step of "realistically modeling a process". It is unclear what limitations applicant intends for a "realistic" progression of cells or for a "realistic" model, or for "realistically" modeling a process, therefore the claims are indefinite. It is noted that various limitations of a "process model" are recited in dependant claims (e.g. 72, 74), however, it is not clear whether these limitations are those which render the model "realistic".

Applicant argues on page 13 of the response that a "realistic" model/system is one which allows practically useful (e.g. clinically) prediction of disease/treatment process and outcome. In response, the examiner maintains that as the goal of a biological model is to duplicate or predict "real-life" events, and thus would be expected to be "useful" in predicting actual responses in organisms (e.g. to a stimulus such as a

drug, to a change in environment, etc.), every model of a biological process may be said to be "realistic" on some level. As there is a vast range of what is defined to be "realistic" in the biological modeling art, applicant's "definition" of a realistic model does not apprise one skilled in the art as to the metes and bounds intended by applicant for a "realistic" system or model. Further, it is noted that none of the claims are directed to a method and system for modeling, NOT to a method of prediction.

Applicant further argues on page 13 of the response that a "realistic" model is one whose structure is "more similar" to "real" physiological system's structure, whose dynamics "more accurately" reproduce a physiological system, and whose parameters have "more direct" physiological meaning and are "more easy" to measure. Applicant does not specify what method, system, model, etc. is used for the comparison for a model which is "more similar", can "more accurately" reproduce a system, has "more direct" meaning, or is "easier" to measure. That is, one skilled in the art would not know what the claimed model is intended to be "more" than by comparison. Further, no standards for comparison are elucidated anywhere, therefore one skilled in the art would not be able to determine what standards are intended by applicant for a model which is "more" or "better" than another at reproducing/modeling a physiological system. It is noted that the claims do not recite a structure for a physiological system, nor a model which reproduces of a physiological system. In addition, applicant does not define what she/he means by a "direct physiological meaning" with regard to parameters. The "definition" set forth at the bottom of page 13 of the response does not apprise one skilled in the art as to the metes and bounds intended by applicant for a

"realistic" model or system, but actually raises more uncertainties with regard to limitations intended by applicant. For all the reasons previously set forth and set forth above, the examiner maintains the rejection.

Claims 75 and 101 recite that a subset of cells release platelets "until they exhaust their capacity" in a limitation of the MK16 compartment. It is still unclear what the "capacity" is which is exhausted, therefore the rejection is maintained.

Claims 76 and 102 have been amended to recite that an process model is "capable of considering" an effect of apoptosis. One skilled in the art generally regards "consideration" to be a thought process; i.e. one which is carried out by a sentient (or near-sentient) organism. Models are not usually regarded as sentient nor capable of "considering" anything. As it is unclear what limitation of the model applicant intends (does applicant truly intend a model capable of thought?), the claims are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 92-94, 97, 100, 114, 341-343, and 346 are rejected under 35 U.S.C. 103(a) as being unpatentable over WICHMANN et al. (Cell Tissue Kinetics (1979) vol. 12, pp. 551-567) in view of THOMAS (US 5,879,673).

Applicant's arguments with respect to claims 92094, 97, 100, 114, 341-343, and 346 have been considered but are moot in view of the new ground(s) of rejection.

WICHMANN teaches a system and method of predicting/modeling thrombopoietic lineage in rats wherein his model comprises a "realistic" progression of cells, specifically through compartments S, M, P, and T (pages 553-554), WICHMANN teaches that his method may be used to model cells involved in thrombocytopenia (pp. 555-556). WICHMANN further teaches that the cells in his compartments may be sub-divided into cells of specific ages (pp. 553-554). WICHMANN also teaches that a

experimental data regarding stem cell proliferation (i.e. bone marrow progression), platelet counts, and TPO concentration changes may be included in his model (p. 555, Table 1). WICHMANN does not teach a model for a general human patient.

THOMAS teaches that models of thrombopoiesis in rodents are "translatable" into human beings; i.e. may be used to model the same disorder/disease in humans. THOMAS also teaches that actual testing of humans is dependent on FDA approval (col. 25, lines 9-22).

It would have been obvious to have translated the model and system of WICHMANN into a system and method to predict thrombopoietic lineage in a human, as suggested by the teaching of THOMAS that rodent models can be translated into human models, where the motivation would have been to model a disease and predict TPO effects in advance or addition to actual human testing, as suggested by THOMAS' teaching that actual testing of humans is more difficult than in silico modeling.

Claims 92-96, 100 and 341-344 are 35 U.S.C. 103(a) as being unpatentable over KLIEM et al. (Experimental Hematology (1997) vol. 25 (8), pp.899) in view of THOMAS (US 5,879,673).

Applicant's arguments with respect to claims 92-96, 100, and 343-344 have been considered but are moot in view of the new ground(s) of rejection.

KLIEM teaches a system/method for modeling/predicting thrombopoietic lineage in mice wherein his system describes in vivo responses, and is therefore "realistic". KLIEM teaches that his system/method can be used to model thrombocytopenia,

comprises data with regard to compartments and transit time of cells (i.e. cell progression), and incorporates the effects of PEG-rHuMGDF administration. KLEIM does not teach a general human patient.

THOMAS teaches that models of thrombopoiesis in mice are "translatable" into human beings; i.e. may be used to model the same disorder/disease in humans. THOMAS also teaches that actual testing of humans is dependent on FDA approval (col. 25, lines 9-22).

It would have been obvious to have translated the model and system of WICHMANN into a system and method to predict thrombopoietic lineage in a human, as suggested by the teaching of THOMAS that mice models can be translated into human models, where the motivation would have been to model a disease and predict TPO effects in advance or addition to actual human testing, as suggested by THOMAS' teaching that actual testing of humans is more difficult than in silico modeling.

Conclusion

No claims are allowed; the specification and drawings are objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

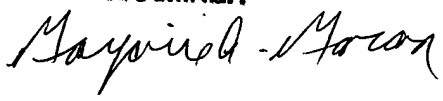
TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER



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